CURRENT TRENDS
IUD SAFETY: REPORT OF A NATIONWIDE PHYSICIAN SURVEY

In an attempt to determine the morbidity and mortality associated with IUD use nationwide, the Family Planning Evaluation Division, CDC, in conjunction with the Committee on Maternal and Child Care of the American Medical Association (AMA) and the American Osteopathic Association (AOA), began a physician survey in June 1973.

From their master files, AMA and AOA provided the names of 34,544 physicians in the United States and Puerto Rico – virtually all physicians who had a primary, secondary, or tertiary interest in obstetrics or gynecology, or a primary interest in family practice, public health, or general preventive medicine. In the last week of June 1973, CDC sent a questionnaire to all physicians on the list inquiring about women who had been hospitalized or had died with possible complications related to the use of an IUD in the preceding 6 months. Physicians were asked to check 1 or more of 8 diagnostic categories for their patients such as complicated pregnancy, uterine perforation, and hemorrhage. After a second mailing of the same questionnaire to physicians who had not responded by August 1, a total of 16,994 responses (49.2%) were received by January 2, 1974. Subsequently, a 1% probability sample was drawn from the 17,550 non-respondents; field officers were successful in obtaining information about IUD complications from 173 of 176 practices by telephone and personal interviews.

Physicians responding by mail provided 3,502 net, unduplicated case reports of women hospitalized in the first 6 months of 1973. After correction for the non-respondent physicians, approximately 7,900 IUD-associated hospitalizations were estimated to have occurred in this period. Using an estimate by the Family Planning Evaluation Division of approximately 3.2 million IUD wearers in early 1973, the calculated rate of IUD-related hospitalizations was 5 per 1,000 woman-years of IUD use.

While the small number of IUD-related deaths is insufficient to demonstrate an increased mortality rate associated with any specific type of device, the overall rate of IUD-related mortality appears to be low compared with the mortality rates associated with pregnancy and other forms of contraception *(1)*. Five fatalities were reported in the 6-month study period by the 16,994 physicians who responded by mail and the documenting details of each of these cases supported the suggestion that an IUD had contributed to the death. Four of the 5 terminal illnesses involved severe infection; 2 of these 4 infections involved a pregnancy. The devices used by these women were

IUD Safety — Continued

2 Lippes Loops*, 2 Saf-T-Coils*, and 1 Dalkon Shield*. These 5 reports imply a minimum IUD-related mortality rate of approximately 3 per million woman-years of use.

Of the 3,473 reports which included diagnoses, 2,932 also specified the type of IUD involved. A relative excess of Dalkon Shield IUDs was observed among case reports carrying the diagnosis of "complicated pregnancy" (Table 1). The crude odds ratio** for all the cases in Table 1 is 2.1 ($p<.001$). Separate stratifications by the patient's age, race, and geographic region show a comparable elevation of the same odds ratio for each group. When the case reports were stratified by the size of IUD, the odds ratio for the 180 women with nulliparous-sized IUDs was not significantly different from 1.0, but was 2.0 and 2.2 for the parous (standard) and unknown sizes, respectively, both statistically significant.

Table 1
Association Between the Dalkon Shield and Complicated Pregnancies Among Women Hospitalized for IUD-Related Complications*

	Type of IUD					
Diagnosis of Complication	**Dalkon Shield**		**All Other IUDs (incl. Unknown)**		**Total**	
Pregnancy Related	538	(53.9%)	461	(46.1%)	**999**	**(100.0%)**
Not Pregnancy Related	887	(35.9%)	1,587	(64.1%)	**2,474**	**(100.0%)**
Total	**1,425**	**(41.0%)**	**2,048**	**(59.0%)**	**3,473**	**(100.0%)**

*Table excludes 29 case reports with unknown diagnosis.

The 1% sample of non-respondent physicians who were interviewed in person or by phone furnished 60 unduplicated case reports. The crude odds ratio for these reports was 8.3 ($p=.0049$), establishing that a statistical association between the Dalkon Shield and complicated pregnancies also existed in the experience of these physicians.

Since the use prevalence of the various IUD types in early 1973 is unknown, it is impossible to draw any firm conclusion about the morbidity rates associated with each device. The magnitude of the odds ratio is influenced not only by the relatively large number of Dalkon Shields involved in complicated pregnancies (numerator of the odds ratio) but also by the relatively small number of Dalkon Shields involved in complications in non-pregnant women (denominator of the odds ratio). If the Dalkon Shield accounted for more than 41% (Table 1) of the IUDs in use early in 1973, then the observed elevation in the odds ratio might be better explained by a relatively low rate

*Inclusion of trade names does not imply endorsement by the Public Health Service or the U.S. Department of Health, Education, and Welfare.

$$** \quad Odds\ Ratio = \frac{\left(\frac{Dalkon\ Shield}{All\ Other\ IUDs}\right)\ pregnancy\ related}{\left(\frac{Dalkon\ Shield}{All\ Other\ IUDs}\right)\ not\ pregnancy\ related}$$

IUD Safety — Continued

of hospitalizations for non-pregnant complications associated with this type of IUD. Such a high use prevalence of the Dalkon Shield is very unlikely based on CDC's review of sales data furnished by the major IUD manufacturers. The relative excess of women hospitalized with complicated pregnancies associated with the standard-sized Dalkon Shield could possibly be explained by an elevated rate of pregnancy with this device, by an increased rate of complications once a pregnancy is established, or by a combination of these postulated factors.

(Reported by the Committee on Maternal and Child Care of the American Medical Association; the American Osteopathic Association; and the Family Planning Evaluation Division, Bureau of Epidemiology, CDC.)

Reference

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Editorial Note—1997: Since the mid-19th century when Ignaz Semmelweiss, Oliver Wendell Holmes, and others showed that puerperal fever was both contagious and preventable, epidemiology has been useful as an effective tool to assist in improving reproductive health. CDC first applied epidemiology to family-planning evaluation and reproductive health in the early 1960s when new female fertility-control measures had become available. Oral contraceptives and plastic intrauterine contraceptive devices (IUDs) provided promising new opportunities for family planning. CDC leaders, especially Alexander D. Langmuir, M.D., Chief Epidemiologist, had both enthusiasm and concern about these opportunities. Evidence for the effectiveness of the new methods of contraception was emerging, but potential adverse effects remained largely unevaluated. Of specific concern to Langmuir was the possible relation between IUD use and pelvic infection. Therefore, in 1964, CDC assigned Nicholas Wright, M.D., an officer in CDC's Epidemic Intelligence Service (EIS) program, to Grady Memorial Hospital, a public institution in Atlanta, Georgia, with a large ambulatory-care clinic and approximately 1000 beds, to investigate the safety of the IUD. Work by Wright and others determined that women with IUDs had pelvic infections at a higher rate than expected but that most of these women could be treated effectively and without serious complications.

A decade later, the *MMWR* of June 29, 1974, raised questions about the safety of the Dalkon Shield, an IUD marketed during 1970–1974. Both the AMA and the AOA collaborated with CDC to conduct this survey of physicians in June 1973. Analysis of the case reports supplied by the survey respondents showed an excess risk for complicated pregnancies among Dalkon Shield users, compared with users of other IUDs (*1*). In 1974, the manufacturer withdrew the device from the marketplace.

In 1975, CDC reported that Dalkon Shield users were more likely than users of other IUDs to die from spontaneous abortions (*2*). Reports of mid-trimester septic abortions associated with the Dalkon Shield hastened the passage of the Medical Device Amendments of 1976, which gave the Food and Drug Administration (FDA) greater control over medical devices. In 1983, CDC reported that Dalkon Shield users had a greater risk for pelvic inflammatory disease than users of other types of IUDs and non-IUD users (*3*). In that same year, CDC and FDA recommended that women still using Dalkon Shield IUDs have them removed. The experience with the Dalkon Shield has had a dramatic negative impact on the further use of IUDs in the United States and

IUD Safety — Continued

has affected the pharmaceutical industry, physicians, and women who otherwise might find the IUD an acceptable method of contraception (*4,5*).

IUDs, first used in Germany and Japan in the early 1900s, showed great promise after their reintroduction in 1960 as biologically inert plastic devices (*6*). Thereafter, a large variety of devices were produced as manufacturers attempted to identify the ideal device. The most important recent advance was the development of the medicated devices, particularly the copper-bearing IUDs (*7*). The most commonly used IUD in the United States today—the Copper T380A—has a low rate of side effects and is perhaps the most effective IUD in use internationally, with a pregnancy rate of ≤1% per year (*8*). In Europe, the levonorgestrel-releasing device also is associated with few side effects, very low failure rates, and reduced menstrual blood flow because of intrauterine progestin effect (*9*). This device has not been introduced into the United States. As a result, the only progesterone-releasing device available in the United States requires change of the device annually and is rarely used in this country.

During the 1980s, the noncopper-bearing devices popular in the 1960s and 1970s were withdrawn from the market for economic reasons (*4*). In 1986, manufacturers also removed copper-bearing devices from the market—not because of new information about risks, but because of the heavy financial burdens imposed on the manufacturers by issues related to liability (*4*).

The major safety concern associated with the use of IUDs has been the risk for developing pelvic inflammatory disease (*10*). Recent studies have suggested, however, that most cases of pelvic infection that occur with an IUD in place are attributable to sexually transmitted diseases (STDs) (*11,12*) and that women at low risk for STDs also are at low risk for pelvic infection while they are using an IUD. Further evidence that the IUD is associated with low risk for pelvic infection is documented by a study of infertility in which IUD users with one sexual partner were at no greater risk for infertility than nonusers of the IUD (*13*). Most IUD-attributable infections appear to be related to insertion of the device (*12*); some of these infections probably are preventable with proper infection-control measures, and trials of the effectiveness of administering prophylactic antibiotics at the time of insertion are in progress.

The 1974 *MMWR* and subsequent reports by CDC identified an increased risk for infectious morbidity related to use of an IUD that is no longer marketed. Subsequent epidemiologic studies of the safety of currently available devices indicate that women at low risk for STDs are at low risk for pelvic infection with IUD use.

In the United States, nearly 60% of pregnancies are unintended (*14*), and many women wanting to prevent unintended pregnancy are appropriate candidates for IUD use. Despite evidence that the long-term effectiveness of the Copper T380A device is similar to that of tubal sterilization (*15,16*), <1% of women using contraceptives in 1995 were using this device (*17*). Among the small number of women using IUDs, however, acceptance of this method is high: in 1992, for example, 96% of IUD users viewed their method favorably, compared with 94% of oral contraceptive users, 93% of those who chose male or female sterilization, 76% of diaphragm users, and 74% of rhythm methods users (*18*). Women desiring long-term effective contraception and their clinicians should be aware that currently marketed IUDs are highly effective and acceptable and are associated with a low risk for complications in women at low risk for STDs.

IUD Safety — Continued

In addition to highlighting the commemoration of CDC's 50th anniversary, reprinting this 1974 *MMWR* coincides with and highlights the 30th anniversary of CDC's Division of Reproductive Health. In 1967, the Family Planning Evaluation Activity (FPEA)—which authored the 1974 report—was established in CDC's Bureau of Epidemiology, becoming one of CDC's earliest noninfectious disease program areas. The FPEA began with only four staff members; today, the staff consists of 160 members in what is now the Division of Reproductive Health, part of CDC's National Center for Chronic Disease Prevention and Health Promotion. In 1970, the FPEA became the Family Planning Evaluation Division, and the division quickly became a focus of excellence within CDC, helping to introduce and disseminate further the concepts of analytic epidemiology eventually adapted by acute/infectious disease programs. From 1967 (when the division first assigned EIS officers to evaluate family-planning programs in state health departments) to the present, the links between the division and the EIS have been crucial at CDC in helping to introduce CDC's methods of applied/field epidemiology to the challenges of reproductive health, both nationally and internationally. The three decades of history of the division reflect the creative and effective use of epidemiology for the promotion of reproductive health.

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IUD Safety — Continued

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